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Original article

Anal and rectal function after intensity-modulated prostate radiotherapy with endorectal balloon

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ABSTRACT

Background and purpose: Late anorectal toxicity influences quality of life after external beam radiotherapy (EBRT) for prostate cancer. A daily inserted endorectal balloon (ERB) during EBRT aims to reduce anorectal toxicity. Our goal is to objectify anorectal function over time after prostate intensity-modulated radiotherapy (IMRT) with ERB.

Material and methods: Sixty men, irradiated with IMRT and an ERB, underwent barostat measurements and anorectal manometry prior to EBRT and 6 months, one year and 2 years after radiotherapy. Primary outcome measures were rectal distensibility and rectal sensibility in response to stepwise isobaric distensions and anal pressures.

Results: Forty-eight men completed all measurements. EBRT reduced maximal rectal capacity 2 years after EBRT (250 ± 10 mL vs. 211 ± 10 mL; $p < 0.001$), area under the pressure–volume curve (2878 ± 27 0 mL mmHg vs. 2521 ± 305 mL mmHg; $p = 0.043$) and rectal compliance (NS). Sensory pressure thresholds for first sense and first urge (both $p < 0.01$) increased. Anal maximum pressure diminished after IMRT ($p = 0.006$).

Conclusions: Rectal capacity and sensory function are increasingly affected over time after radiotherapy. There is an indication that these reductions are affected less with IMRT + ERB compared to conventional radiation techniques.

Late gastrointestinal side effects have an important impact on quality of life after external beam radiotherapy (EBRT) for localized prostate cancer [1]. Up to 50% of patients after EBRT report late gastrointestinal symptoms and some studies report that in 90% of patients changes in their bowel habits are reported [2]. Most often these symptoms are mild and, fortunately, more severe symptoms interfering with quality of life (QoL) are less frequently seen. Recently, a percentage of approximately 3% is reported for severe gastro-intestinal symptoms (EORTC grade $\geq$3) [3]. Symptoms of late gastrointestinal toxicity comprise rectal blood loss, increased stool frequency, loose stools, fecal urgency and fecal incontinence [4,5]. Reduction of these side effects will help to improve QoL after treatment [6,7]. Especially complaints such as fecal incontinence and fecal urgency have a large influence on QoL [8].

At this moment, the underlying pathophysiology of late anorectal toxicity is poorly understood. Prior studies showed that there is a relation between radiation dose to the anal wall and rectal wall on the one hand, and the frequency and severity of late toxicity on the other [9–11]. Associations between anorectal dose and anal and rectal functions, especially rectal capacity, rectal sensibility and anal pressures have recently been found [12–14].

Improvements in radiation techniques, such as intensity modulated radiotherapy (IMRT), volumetric arc therapy (VMAT) and image-guided EBRT, enable better sparing of healthy structures and tissues [15,16]. Unfortunately, due to the close anatomic relation between the rectum, anal canal and the prostate, it is still impossible to completely spare the rectum and anal canal. Several methods have been developed to increase the distance between the prostate and the anorectum, including a daily inserted endorectal balloon (ERB) during EBRT. The ERB pushes the lateral and posterior rectal walls out of the high dose radiation volume, with the aim to reduce anorectal toxicity [17,18]. Prospectively collected data on anorectal function after EBRT with state-of-the-art radiation techniques combined with a daily inserted ERB are scarce.

Currently available publications on late anorectal function after prostate radiotherapy report on relatively small patient cohorts of around 30 patients [12,19,20]. A few studies included significantly

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more patients, but these (1) were of retrospective or cross-sectional design, or (2) included heterogeneous patient cohorts including prostate, cervical and rectal cancer, or (3) used outdated radiation techniques [16,21,22].

So far, only one study used electronic barostat measurements to assess rectal capacity and compliance [12], while barostat is currently seen as the most reliable test to explore rectal pressure–volume relations [23,24].

Therefore, the primary aim of this study is to describe changes over time in anorectal function up to two years after state-of-the-art EBRT using objective function tests, in a large group of men irradiated with image-guided intensity modulated radiotherapy and a daily inserted ERB for localized prostate carcinoma.

Materials and methods

Study design

This study is a prospective and longitudinal cohort study with a pretest–posttest design. All patients underwent anorectal function testing prior to EBRT (baseline), 6 months, 1 year and 2 years after EBRT.

Primary outcome measures consist of rectal distensibility (rectal capacity, rectal compliance and area under the pressure–volume curve), rectal sensibility and anal pressures.

The local ethics committee approved the study protocol and all patients had to give informed consent before inclusion into the study.

Patients and treatment

All patients who were to receive EBRT in the Radboud University Medical Center for localized prostate cancer (T1c-3bN0-1M0) between November 2009 and May 2012 were invited to take part.

Patients who had prior radiotherapy, major abdominal surgery or inflammatory bowel disease in their medical history were excluded.

All patients received IMRT with a cumulative radiation dose of 64.6–78 Gy in 2.0–3.4 Gy fractions and a daily inserted ERB. A more detailed overview of patient-, tumor- and treatment characteristics is given in Table 1.

Anal and rectal function tests

To measure rectal distensibility and sensibility an electronic barostat (Distender II, G&J Electronics Inc., ON, Canada) was used. Anal pressures were measured by manometry with a Solar GI system (MMS, Enschede, The Netherlands). A detailed description of techniques can be found elsewhere [12,25,26].

In short, a single-use infinitely compliant barostat catheter is used. A rectal staircase distension is performed starting at an intrabag pressure of 0 mmHg. At one-minute intervals the intrabag pressure is increased by 2 mmHg and kept constant. Intrabag volumes are averaged beginning 25 s at each distension step. Both the pressures and volumes at each distension step were recorded. Maximum distension was noted the moment a patient encountered a strong feeling of discomfort or an uncontrollable urge to defecate. For safety, the maximum distension was limited to 48 mmHg.

Three different parameters were used to reflect rectal distensibility: (1) rectal capacity, (2) rectal compliance and (3) the area under the pressure–volume curve (AUC). Rectal capacity is the volume, measured at the maximum tolerated distension (or 48 mmHg). Rectal compliance is the maximum slope (ΔVolume/ΔPres sure) of the pressure–volume curve. The AUC is the area under the pressure volume curve. This curve is divided into separate distension steps. The AUC represents the sum of all individual distension steps. The area of each distension step was calculated by the formula:

Area distension step = $\text{Vdistension}_{(i)} \cdot 2\ \text{mmHg} + 0.5 \cdot 2\ \text{mmHg} \cdot (\text{Vdistension}_{(i+1)} - \text{Vdistension}_{(i)})$,where i is distension step number and V is volume at i-th distension step.

If maximum distension steps at the various time points were different for one patient, the AUC was calculated up to the lowest maximum distension step for this patient [12].

Rectal sensibility was measured by use of 3 sensory thresholds: (1) first sense (the first moment a patient became aware of any sensation in the rectum), (2) first urge (the first moment a patient experienced urge) and (3) maximum tolerated distension (the moment a patient encountered a strong feeling of discomfort or an uncontrollable urge to defecate). During barostat measurements distension steps corresponding to the sensory thresholds were noted.

Anal pressures were measured by anal manometry. A standard station pull-through technique with a water-perfused 4-channel 14 French single use catheter was used to determine anal resting

Table 1
Characteristics of patients and tumor characteristics prior to radiotherapy ($n = 60$).

Characteristics	Mean	SD	n	(%)
Patient characteristics				
Age (years)	69	5.8		
Length (cm)	176	6.0		
Weight (kg)	84	11.4		
BMI (kg m^{-2})	27.0	3.2		
Tumor characteristics				
PSA (range)	15.8	(2.1–93)		
Gleason (median; range)	7	(6–9)		
T-stadium				
T1			4	(7)
T2			18	(30)
T3			38	(63)
Treatment characteristics				
Adjuvant hormonal therapy			31	(52)
Radiation dose (cumulative dose/fraction dose)				
64.6/3.4 Gy			21	(35)
70/2.5 Gy			27	(45)
78/2.0 Gy			12	(20)

Abbreviations: BMI, Body Mass Index; PSA, prostate specific antigen; T-stadium, tumor stadium; Gy, Gray.

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